

C H L O R I D E M E T A B O L I S M

WITH SPECIAL REFERENCE TO THE EFFECT ON GASTRIC SECRETION OF DIETS DEFICIENT IN CHLORIDES.

INTRODUCTION.

The writer was induced to undertake this investigation by having his attention drawn to the great frequency of gastric disease among the Northern Chinese. Anyone who has practised medicine in North China for even a short time will agree that chronic gastritis and dyspepsia are responsible for a very large proportion of the total number of cases of ill health which he sees from day to day. For instance, the statistics of Mukden Hospital for 1923⁽¹⁾ show that twelve per cent of the outpatients suffered from some kind of chronic gastric disease.

Several reasons might be stated which may account for this fact.

Firstly, the Chinese method of eating is undoubtedly a potent cause of gastric disease. The rapidity with which the average Chinese can consume several large bowlfuls of millet and other vegetables is a

constant source of astonishment to the foreign resident in China. The food is gulped down in huge mouthfuls with only the slightest effort at mastication.

Then again the commonly used diet is largely vegetarian and consequently bulky, thus tending to cause gastric dilatation.

These two factors in themselves are probably sufficient to account for most of the enormous toll which gastric disease takes of the health of the people of Northern China, but it was the possibility of the existence of another cause which prompted the writer to undertake this investigation.

There is one important respect in which the diet of the average Chinese differs greatly from that of the Western races, and that is in the amount of Sodium Chloride consumed with the food. Salt is a government monopoly in China, which fact naturally causes this important article to be considerably dearer than it would otherwise be. As a result, the great mass of the people, who live just above the border line of poverty and starvation are extremely sparing in the use of salt. The staple articles of food are "kao liang" grain (sorghum) and the various kinds of millet, and these are consumed without the addition of salt. A certain amount of salt is taken with green vegetables and as an ingredient of various sauces, but

there is no doubt that the amount of salt consumed daily is very much less than that used by Western races.

It is generally agreed by physiologists that the hydrochloric acid of the gastric secretion is derived from the sodium chloride of the blood plasma, which in turn, is supplied by the food chlorides. It is conceivable that a deficiency in the salt consumed with the food might cause a diminution in the amount of hydrochloric acid secreted by the gastric glands, and might thus contribute to the great frequency of gastric disease among the Chinese. It was for the purpose of investigating this possible factor that the writer undertook the present investigation.

METABOLISM OF CHLORIDES.

Sodium Chloride is one of the most important inorganic compounds in the body and is essential to life. It differs from all other inorganic salts in that the amount contained in the ordinary articles of diet is insufficient to satisfy the needs of the organism, although almost without exception animal and vegetable foods contain considerable amounts of the salt. The other inorganic salts which the body requires are all contained in adequate amounts in a

good mixed diet, whereas the facts that the people of nearly every race of mankind prefer a diet to which salt has been added, and that many animals show a keen appetite for salt, seem to indicate that the addition of salt to the food is essential to complete physical fitness.

Chlorides taken by the mouth are absorbed from the alimentary canal and pass into the blood. The amount of chlorides contained in normal blood has been determined by various observers as follows:-

Rumpf ⁽²⁾	0.44 per cent of whole blood			
Georpulos ⁽³⁾	0.6 - 0.7	"	"	"
McLean and Van Slyke ⁽⁴⁾	0.49	"	"	"
Host ⁽⁵⁾	0.44 - 0.48	"	"	"

The chlorides exist mainly in the plasma, and to a much less extent in the corpuscles.

The concentration of chlorides in the blood is remarkably constant and does not readily alter in spite of changes in the intake of chlorides by the mouth, any excess of chlorides in the blood being rapidly excreted by the kidneys which, as is well known, are extremely sensitive to changes in the concentration of salts in the blood. Ambard and Weil⁽⁶⁾ state that the threshold value for chlorides in the blood is .562% and that when the concentration falls

below this, the excretion of chlorides by the kidneys ceases.

One important function of the blood chlorides is to provide the hydrochloric acid of the gastric secretion. It is certain that the hydrochloric acid of the gastric juice is derived ultimately from the food chlorides. Kulz⁽⁷⁾ and others have proved this by substituting Bromides and Iodides for the Chlorides of the diet and found that the hydrochloric acid of the gastric secretion was replaced by hydrobromic acid and to a less extent by hydriodic acid. The method by which the formation of hydrochloric acid by the gastric glands is effected is not yet determined, although numerous theories have been propounded to explain how a strongly acid fluid such as the gastric juice is, can be derived from an alkaline fluid, viz. the blood plasma. It is not within the scope of this thesis to enter into a discussion of these theories.

The hydrochloric acid secreted by the stomach, after performing its duty as an aid to gastric digestion, is re-absorbed from the intestines in the form of chlorides (organic and inorganic) and re-enters the blood stream. It is thus conceivable that the same chlorides might continue to be used indefinitely were it not for the excretion of part of them by the kidneys and through other channels.

EXCRETION OF CHLORIDES.

This takes place mainly through the kidneys, though a small portion is excreted by the skin and the intestines. In health, any excess of chlorides is excreted rapidly, provided that the intake does not surpass a certain upper limit. Normally, on a regular diet, the amount passed in the urine corresponds fairly accurately to the amount consumed. Advantage has been taken of this fact in connection with the experiments on subjects on a low chloride diet to keep a check on these subjects and ensure that they were not surreptitiously consuming salt.

AMOUNT OF CHLORIDES REQUIRED DAILY.

The average European adult consumes from ten to twenty grams of sodium chloride per day. The present investigation shows that the average Northern Chinese uses from six to thirteen grams daily. There is no doubt that these amounts are greatly in excess of the actual requirements of the organism. Thus, on experimental diets, the amount of salt used can be greatly reduced without evident injury to the body. For instance, Mayer found by experiments made on himself that it was possible to live and feel well on 1.25 grams per day - at least for some weeks. The present

investigation shows that many Chinese use normally less than five grams per day and thrive on it. Bunge⁽⁸⁾ thinks that the organism requires one or two grams of chlorides per day on ordinary diets.

It is well known that the amount of salt used by people of different races varies greatly, and it is generally believed that vegetarian races consume more salt than meat eating races. Widal and Javal state that tribes still leading a nomadic life do not use salt, and that they begin to do so only after they settle down and follow agricultural pursuits. Many other authors agree that in civilised races, vegetarians use more salt than those who include meat in their dietary. Bunge⁽⁹⁾ states that in France, country people consume three times as much salt per head as city dwellers, the assumption being that in the country the average diet contains a larger proportion of vegetables. Bunge explains this by the fact that vegetables contain considerable quantities of potassium salts - especially potassium carbonate - which reacts in the body with sodium chloride, forming sodium carbonate and potassium chloride. The sodium carbonate is excreted, while the potassium chloride is retained. To compensate for the loss of sodium, vegetarians are inclined to use more salt in their food. This theory is questioned by several

authors, and there are certain facts which seem to throw doubt on it, such as the existence of a sect of vegetarians at Locarno mentioned by Forel, who use no salt, and the fact that certain herbivorous animals, for instance the hare and the rabbit, show no appetite for salt. Lapique⁽¹⁰⁾ discovered some African races living on vegetable substances alone and using the ashes of the plants, which contain more potassium than sodium, as civilised persons use ordinary salt. He holds therefore that salt is of value only as a flavouring agent. Bunge⁽¹¹⁾ states that in countries where the natives live mainly on rice and meat, there is no craving for salt. He explains this by the fact that rice contains only a small amount of potassium, viz. only one sixth as much as wheat, rye, barley and Indian corn, and only one twentieth as much as legumes and potatoes.

In North China, the staple article of diet is kaoliang grain (sorghum). The amount of potassium in this grain has not been determined. The writer has estimated the chlorides in sorghum at .25 per 1000 parts.

Fresh vegetables are also largely used, but very little meat, except at feast times.

It will be shown that the amount of salt used by the Northern Chinese is comparatively small. It

is difficult to determine whether this is due to a relative absence of appetite for salt or to the expensiveness of this commodity. However, the fact that most foreigners who eat Chinese food find the use of additional salt desirable, tempts one to imagine that the latter reason is the more likely.

THE GASTRIC SECRETION IN HEALTHY CHINESE.

The first step was to determine the hydrochloric acid content of the gastric secretion in normal Chinese subjects. To the best of the writer's knowledge, this has never been done in the case of Northern Chinese, and it is undoubtedly most desirable that the normal standards should be determined, both from the point of view of scientific interest and also as a necessary preliminary to a study of pathological conditions of the gastric secretion in Chinese patients.

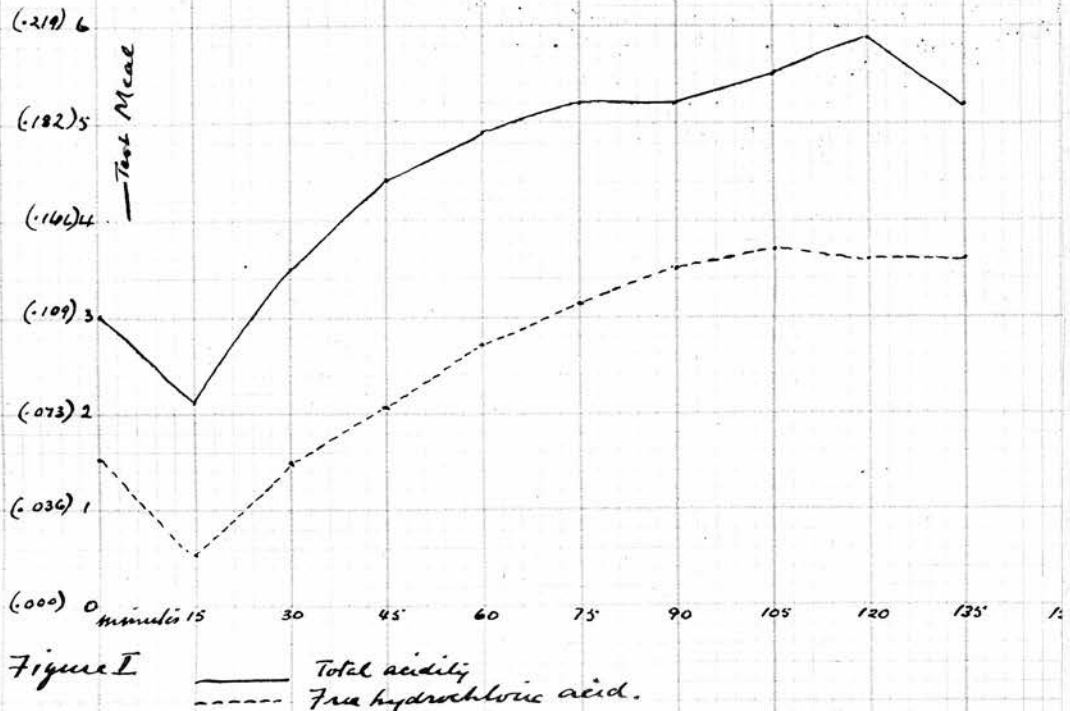
For this purpose a series of estimations was made of the gastric secretion of young male adults. The subjects of these experiments were mostly students, and hospital nurses and attendants between the ages of fifteen and thirty, and were all healthy and vigorous young men. The method employed was to withdraw the gastric fluid by means of a Rehfuß tube at

intervals of fifteen minutes, the test meal used being the Ewald meal. The Rehfuß fractional method was used in the belief that it affords the most accurate information possible regarding the gastric secretion, and also enables one to avoid errors due to hasty or delayed secretion such as are liable to occur when using the old form of stomach tube. The acidity was estimated in the usual way by titrating with deci-normal sodium hydroxide, using Töpfer's reagent and phenol-phthalein as indicators for free hydrochloric acid and total acidity respectively.

Unfortunately the number of estimations was not so large as could be desired, and this remark applies to most of the experiments performed during this investigation. There is a certain difficulty in persuading healthy individuals to submit to the passing of a stomach tube, with the slight discomfort involved. Still, even the comparatively limited number of experiments made is sufficient to enable certain deductions to be made.

The main result of these experiments is to prove that the hydrochloric acid content of the gastric secretion in normal Chinese does not differ to any great extent from that of normal Europeans. The results are shown graphically in the accompanying figure (Fig. 1) which is a composite curve representing

an average of the results obtained in the twenty-four cases examined.



It will be seen that the maximum concentration of free hydrochloric acid during the period of secretion amounted to 1.34 gm. per litre, while that of total acidity amounted to 2.15 gms. per litre, figures which fall within the limits considered normal by most authorities. The general shape of the curve also resembled closely the average curve in healthy Europeans.

The resting fluid in sixteen cases showed an average of 67 ccs.

URINE CHLORIDES IN HEALTHY CHINESE.

With a view to determining approximately the chloride content of the diets of the subjects of these experiments, the urinary chlorides were estimated. It is generally agreed that the amount of chlorides excreted in the urine bears a close relationship to the amounts ingested in the food. Advantage was taken of this fact in order to obtain a rough estimate of the chloride intake. The subjects of the experiments were on a regular diet, with very slight variations from day to day. It was found that the average daily amount of chlorides excreted was 12.8 grams, calculated as sodium chloride. There was thus no deficiency of sodium chloride in the diets of these subjects. It must, however, be taken into account that all those subjects were members of institutions - either medical college or hospital - and that therefore their diet was probably different from that of persons not attached to such institutions.

Accordingly, the urinary chlorides of a series of hospital patients were estimated, in the belief that the results would give a fairer indication of the conditions amongst the general population. In most of the cases, the urine examined was that passed in the twenty-four hours immediately following

admission to hospital. It was found as a result of 34 such estimations that the average daily output of chlorides in the urine amounted to 6.03 grams. If this figure may be taken as a rough estimate of the average daily chloride output of the population at large, it may be compared with the 15 grams usually accepted as an average in the case of Europeans and proves that the average daily consumption of salt by Chinese is very much less.

The following table shows that the largest number of subjects secreted between 5 and 10 grams of sodium chloride daily, and that less than one third excreted more than 10 grams daily.

Amount of Chloride excreted daily as NaCl.	Number of Cases.
0 - 5 gms.	18
5 - 10 gms.	21
10 - 15 gms.	10
15 gms. and over	8

Another fact elicited was that there is no evident correspondence between the hydrochloric acid content of the gastric secretion and the chloride content of the urine.

Subjects with a low chloride content in the

urine and therefore presumably a low chloride intake did not necessarily have a low hydrochloric acid content in the gastric juice, and per contra those with a large amount of urinary chlorides did not necessarily have a high acid content in the gastric secretion.

The following tables demonstrate this point:-

1. Cases in which the daily excretion of Chlorides was less than 5 grams.

Amount of Chlorides excreted daily as NaCl.	Maximum Free HCl in gastric secretion in terms of $\frac{N}{10}$ NaOH.	Maximum Total Acidity in terms of $\frac{N}{10}$ NaOH.
4.53	6.5	7.7
0.73	5.0	6.6
4.85	4.3	5.3
2.10	7.4	8.8
4.60	4.1	5.5
3.19	2.8	5.0
3.05	4.4	6.8
2.75	3.2	5.5
4.48	0.0	2.1
3.65	5.6	8.1
3.46	8.5	11.0
3.14	10.2	11.8
3.14	6.3	8.7
4.60	3.0	5.0
4.49	10.0	11.1
1.10	3.2	4.4
2.65	7.1	8.8
Totals 56.51	91.6	122.2
Averages 3.32	5.4	7.2

2. Cases in which the daily excretion of Chlorides
was more than 15 grams.

Amount of Chlorides excreted daily as NaCl.	Maximum Free HCl in gastric secretion in terms of $\frac{N}{10}$ NaOH.	Maximum Total Acidity in terms of $\frac{N}{10}$ NaOH.
15.72	6.8	9.0
15.65	6.2	8.9
28.13	4.4	6.6
23.38	3.8	5.2
21.93	1.8	3.2
16.82	6.3	13.5
Totals 121.63	29.3	46.4
Averages 20.27	4.9	7.7

These results seem to prove that with ordinary diets, even large variations in the amount of sodium chloride consumed have no effect on the amount of acid secreted by the gastric glands.

EXPERIMENTS WITH SALT FREE DIETS.

Various authors during the last fifty years have described the results of feeding animals on salt-free diets. Some of the more noteworthy of these experiments are here described.

Forster⁽¹²⁾ in 1873 found that an animal fed on a diet without salts died in a shorter time than if it had received no food at all.

Bunge⁽¹³⁾ suggested that this rapid death is due mainly to the production of acids, e.g. sulphuric acid, from proteins, and that death might be postponed for a few days by giving sodium carbonate. This was later proved to be a fact. Animals fed on a completely salt free diet showed disorders of digestion. Towards the end of the experiments they vomited food which showed no signs of digestion even after being in the stomach for some hours. It should be noted that these experiments had no special reference to sodium chloride, all the inorganic salts having been removed. Moreover, it is very probable that Forster in his attempt to remove the salts from the diet also succeeded in removing most or all of the vitamins, the importance of which substances was not recognised at that time. It is likely that most of the symptoms observed and the early death of the animals were due to avitaminosis. It is, however, possible that some of the gastric symptoms were due to the effect of the saltless diet on the gastric secretion.

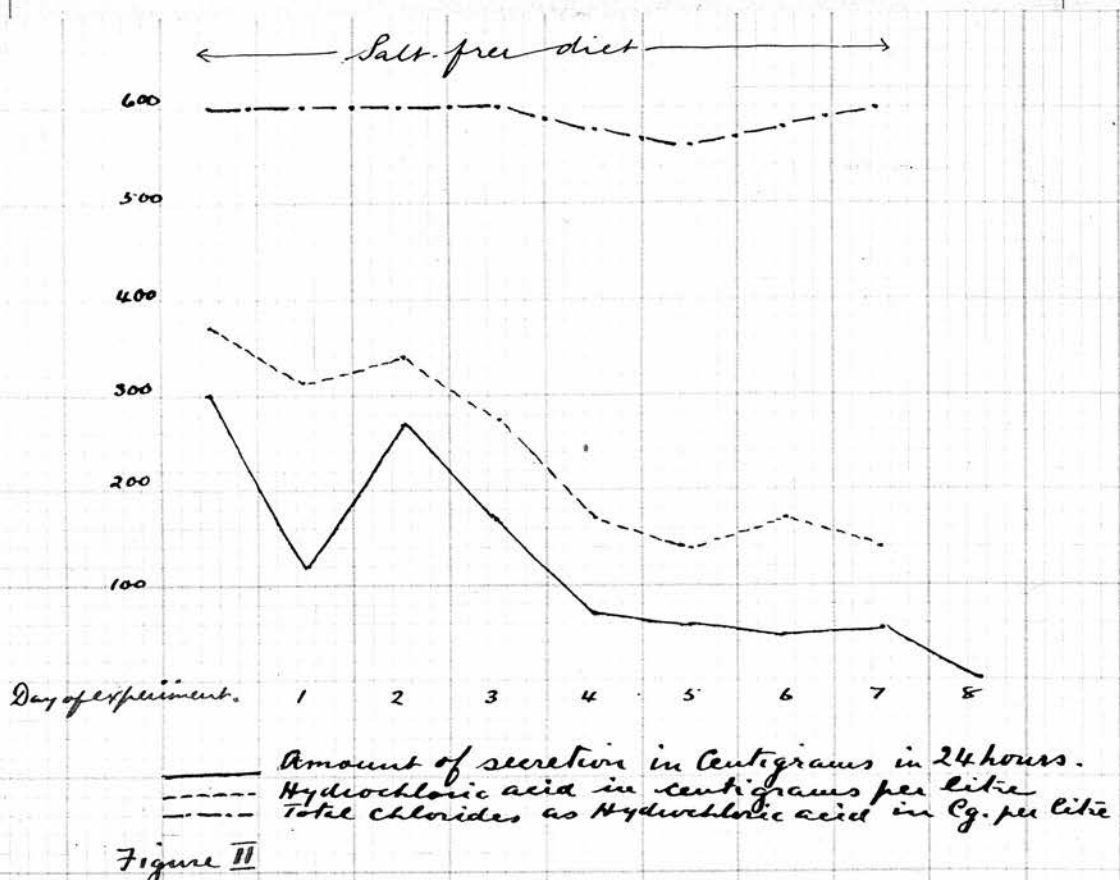
Cahn⁽¹⁴⁾ studied more particularly the effect of a salt free diet on the gastric secretion. His method consisted in feeding animals on a meat diet from which all inorganic salts had been removed by successive boilings. He then added amidon and fat.

He noticed a diminution in the total quantity of gastric secretion and also of the acidity. After some time he found that the gastric secretion was very small in amount and quite neutral in reaction. At this time, there was still a small quantity of chlorides being excreted in the urine. On adding sodium chloride to the diet, he found that the gastric secretion became acid again, and also that the appetite of the animal improved. The results of these experiments, though valuable, are inconclusive. The boiling to which the food was subjected would necessarily remove many of the vitamins and also the extractives. The stimulant effect of these on the gastric secretion is undoubted.

Frouin⁽¹⁵⁾ in 1899 performed a series of experiments which produced more trustworthy results. He used dogs in which the stomach had been isolated by resection at the cardia and pylorus, the continuity of the alimentary canal being restored by suturing the oesophagus to the duodenum. The diet administered consisted of 500 grams of horse meat and 200 grams of rice cooked in water with 5 to 10 grams of sodium chloride. On this diet, the animals remained in good health. If the sodium chloride was then omitted from the diet, Frouin found that by the seventh or eighth day the gastric secretion was

entirely absent. This result was constant in all his experiments. The percentage acidity of the fluid also decreased, but the concentration of total chlorides was practically unaltered, varying only from 5.85 to 6.13 grams per litre. This means, of course, that the absolute amount of chlorides decreased pari passu with the decrease in the amount of gastric secretion, until it reached zero. Parallel with the decrease of the gastric secretion, there was a progressive loss of appetite, and towards the seventh or eighth day, when the secretion was nil, the animal took scarcely any nourishment.

One of Frouin's charts is reproduced below (Fig. II.).



These striking results must be due to the lack of sodium chloride from the diet, since all other salts, extractives, etc., were left in their normal condition.

These experiments seem to prove definitely that the absence of chlorides from the diet will in a very short time result in the cessation of the gastric secretion. The only possible fallacy lies in the fact that the total gastric secretion was removed daily for examination. Normally, as stated above, the greater proportion of the chlorides which leave the stomach are re-absorbed by the bowel and pass into the circulation again. Very little is excreted in the faeces. The effect of this daily removal of the gastric secretion with its contained chlorides would be to produce the results obtained by Frouin very much more quickly than if the chlorides were left in the organism to be re-absorbed and re-utilized. Frouin recognised this possible fallacy and repeated his experiments, this time removing only one tenth or one fifth of the gastric secretion daily. He obtained similar results, except that it took longer - from eight to twelve days - for the cessation of gastric secretion to occur.

On sodium chloride again being added to the diet, the amount and the acidity of the gastric secretion were

found to increase parallel with the amount of sodium chloride given. For instance, in an animal receiving 3 grams of sodium chloride daily, 180 ccs. of gastric juice were obtained with an acidity of 1.99 grams per litre - with 10 grams of sodium chloride, 520 ccs. of juice were obtained with 3.74 grams of free hydrochloric acid per litre - with 15 grams of sodium chloride per day, the animal secreted 600 ccs. of gastric fluid with 4.15 grams of acid per litre.

Frouin also determined that a concentrated solution of sodium chloride (150 ccs. of 10%) injected directly into the isolated stomach produced an abundant secretion of slightly acid fluid. On the following day, although no more sodium chloride had been given, the stomach secreted a fluid almost similar in amount and acidity to that secreted in an animal receiving a normal amount of chloride by the mouth, and more than that which would be obtained by the addition to the diet of an amount of salt equal to that absorbed by the stomach on the preceding day. He concluded that sodium chloride has a direct action on the gastric mucosa which is manifested at least during the twenty-four hours following the introduction of salt into the stomach.

Frouin then studied the effect of intraperitoneal and intravenous injections of saline solutions (250

ccs. of 0.95% solution) on animals on a salt free diet. The gastric secretion was presumably absent, although this is not definitely stated by Frouin in his article. Following the injection, the animal was left fasting. Frouin succeeded in obtaining from 150 to 180 ccs. of gastric fluid containing from 2.007 to 3.46 grams of free hydrochloric acid per litre.

These results, if accurate, would prove that gastric secretion may be influenced by the chloride content of the blood - apart from any psychical, physical or chemical effect of the introduction of chlorides into the stomach by the mouth.

Using the chlorides of calcium, potassium and magnesium, Frouin obtained results similar to those obtained with sodium chloride. This shows that the effect of these salts on the gastric secretion is due to the chloride ion.

It should be noticed that Frouin's so-called salt-free diet was one which, although free from added salt, still contained the natural sodium chloride of the meat and rice, and thus was not absolutely salt free.

In the light of these results, there seems to be little doubt as to the important role played by the food chlorides in the production of the gastric secre-

tion. The question therefore arises, whether or not these results obtained in the experimental animal can be reproduced in the human subject. If so, are questions of real clinical importance involved? For instance, is a deficiency of salt in the diet, whether due to racial habits or to individual tastes, likely to lead to a diminution in the amount and acidity of the gastric juice, with deleterious effects on the digestion? Or again, when a patient is given a salt-free diet for a considerable period of time, as in the modern treatment of nephritis with oedema, is such a diet likely to lead to dyspepsia? Is it possible to treat hypersecretion or hyperchlorhydria by restricting the food chlorides, or vice versa, to treat a patient with deficient secretion of hydrochloric acid by increasing the chlorides in his food?

In undertaking the present investigation, the writer had no intention of studying the effects on the gastric secretion of absolutely chloride-free diets, as he recognises that such an investigation would not be of direct clinical importance. Chlorides are so almost universally present in articles of diet that it is most unlikely that a dietary, however restricted, should be entirely deficient in chlorides. On the other hand, it is certain that in North China at least many persons habitually exist on diets which

are relatively poor in added chlorides. Are such diets likely to lead to ill health? If so, what is the minimum amount of chlorides required to maintain the body in sound health?

In order to answer such questions, a prolonged investigation of numerous subjects would be necessary, not only with reference to the gastric secretion but to many other organs and functions of the body - for instance, body weight, general well-being, resistance to disease, etc. It is to be regretted that owing to the exigencies of hospital practice in China, such a detailed study has proved impossible, and the writer has had to rest content with the limited problem of the effect of variations of chloride intake on the gastric secretion and secondarily on the urinary chlorides.

EFFECT OF CHLORIDE FREE DIET ON THE URINE.

On a salt free diet or during starvation, the amount of chlorides in the urine falls rapidly during the first two or three days, until a minimum of about 0.6 gram. is reached. Thus Luciani found that in a case of prolonged starvation there was an average daily excretion of 0.66 gram. of sodium chloride from the fourth to the thirtieth day.

Benedikt⁽¹⁶⁾ found that during thirty-one days of starvation there was a total output of 12.27 grams of chlorine, i.e. 20.22 grams of sodium chloride, equivalent to a daily average of 0.65 gram. He considers that this is derived from the tissues, mainly from disintegrated muscle, the result of katabolic changes. Benedikt also believes that since the amount excreted during the thirty-one days amounted to only 12.27 grams, it casts a doubt on the theory held by some that an excess of chlorides is stored in the tissues.

With a view to determining whether or not these results obtained by Frouin could be obtained in the human subject, the author undertook a series of experiments. Here again the difficulty in persuading patients to submit to a salt free diet and to frequent examinations of the gastric secretion was encountered. The method employed was as follows.

The gastric secretion was first examined by the fractional method and the urinary chlorides estimated, the patient being on ordinary diet. The patient was then put on a salt free diet and his gastric secretion and urinary chlorides examined at weekly intervals.

Nine cases were examined in this way. Of these, one showed from the examination of his urinary chlorides that he was surreptitiously consuming large

quantities of salt, and he is thus excluded.

The following Table shows the number of weeks the experiment lasted in the various cases.

No. of Weeks	No. of Cases
5	1
4	1
3	0
2	2
1	4

The following Table shows the effect on the acidity of the gastric secretion.

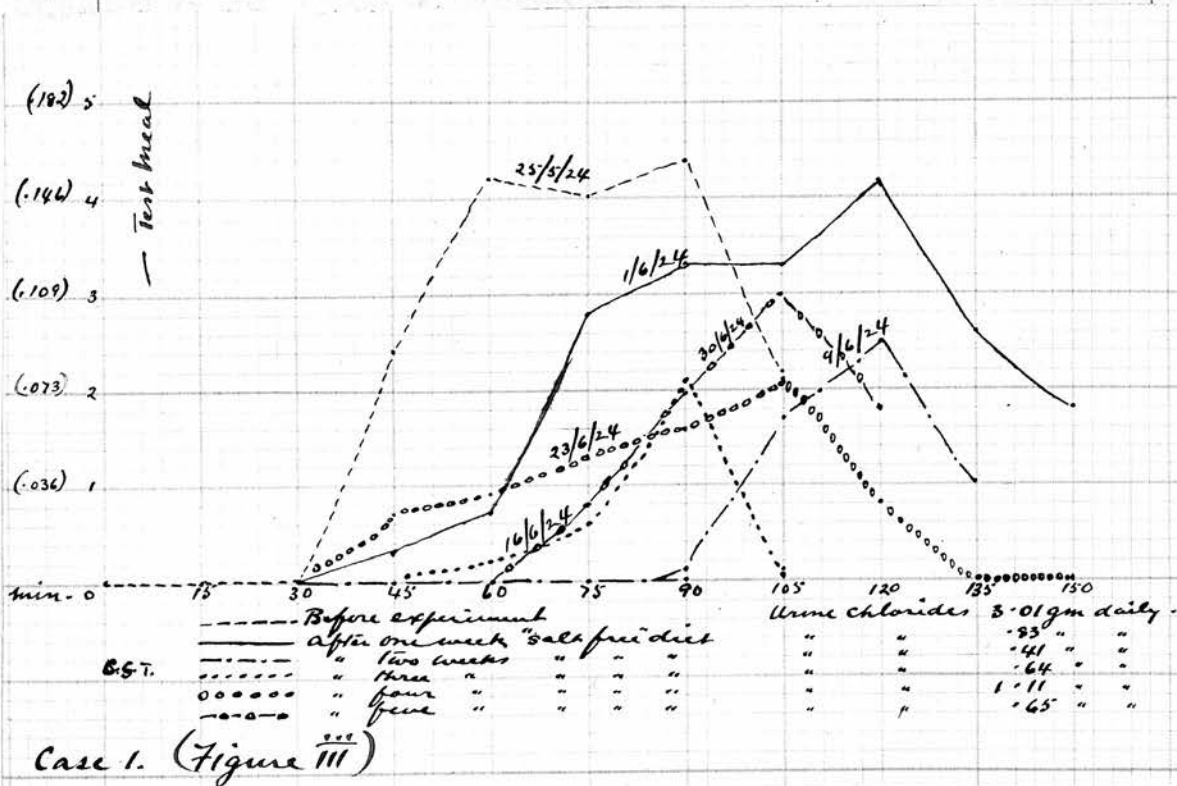
Diminished	Unchanged	Increased
5	2	1

The following Table shows the effect on the acidity of the gastric secretion in relation to the duration of the experiment.

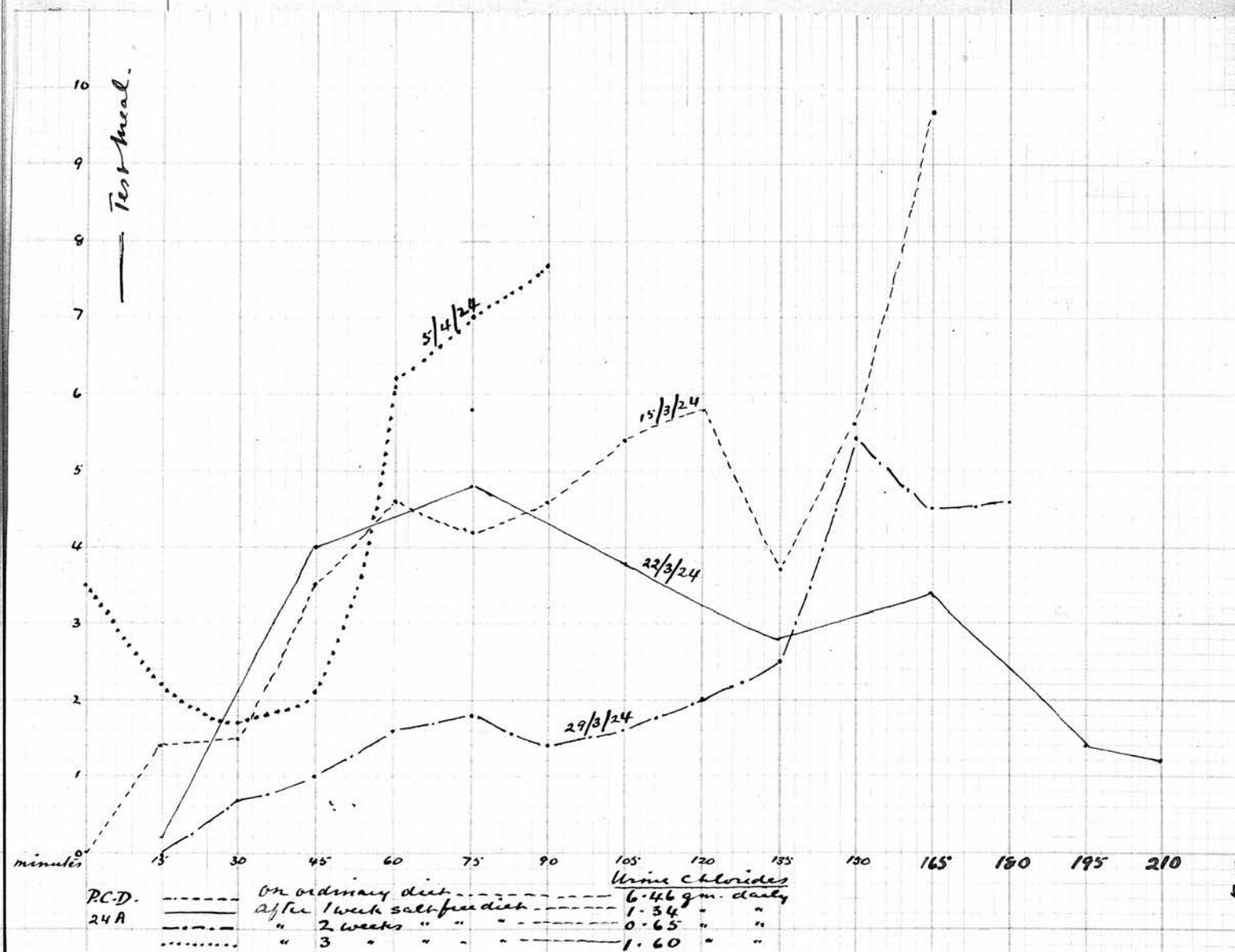
Duration of Experiment	Diminished	Unchanged	Increased
5 weeks	1 Case	-	-
4 "	1 "	-	-
2 "	1 "	-	1 Case
1 "	2 Cases	2 Cases	-

The following figures illustrate the ~~more striking~~ cases graphically.

Case 1. C.S.T. (Fig.III.)



This case was under observation for the longest time. It shows very clearly a diminution of approximately 50% in the free acidity.

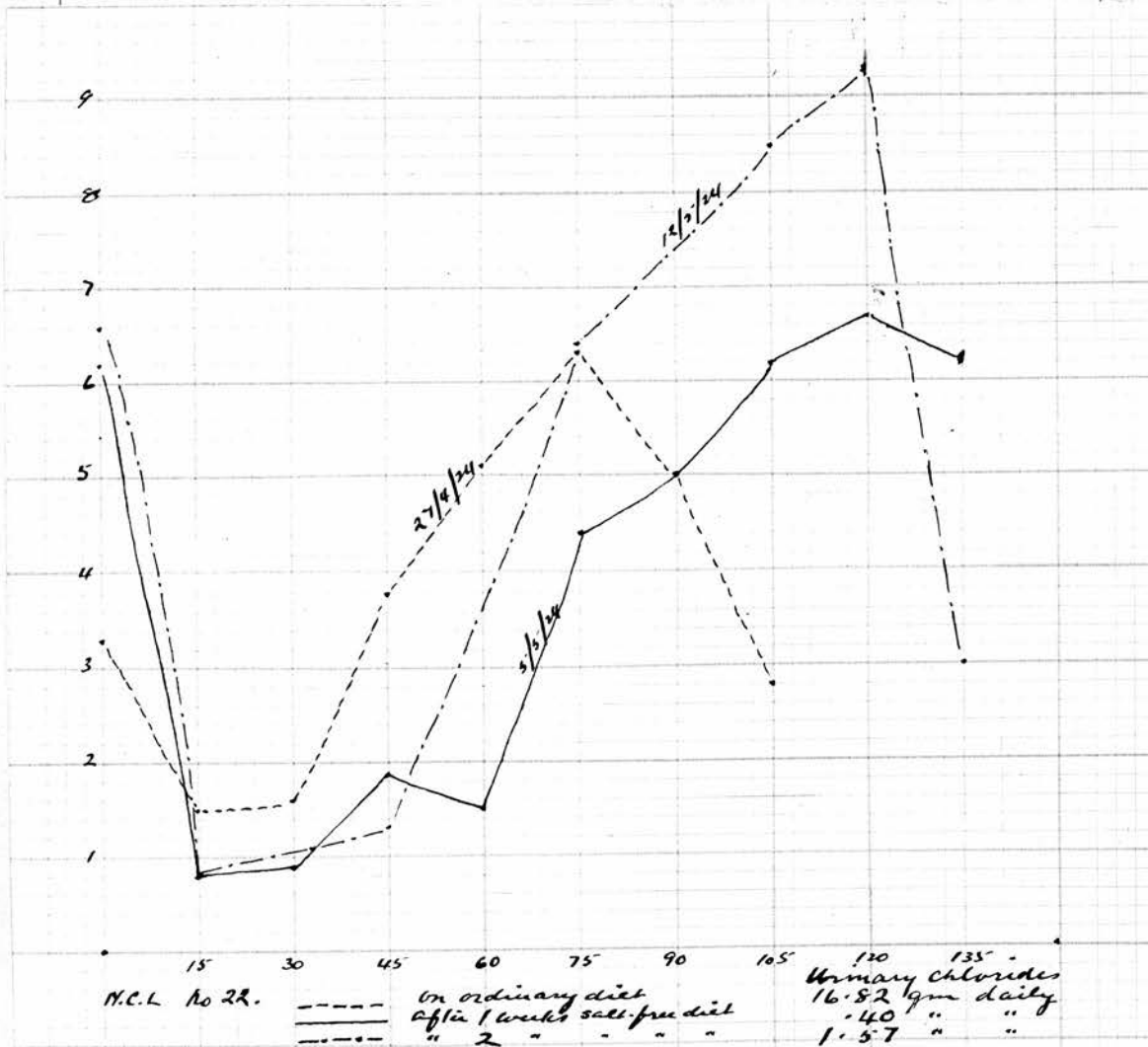
Case 2. P.C.D. (Fig. IV.)

Case 2. Figure IV

This case also shows a diminution in the free acidity of approximately 50% after two weeks on salt free diet, by which time the urinary chlorides had fallen to 0.65 gm. daily. After the third week, the urinary chlorides had risen to 1.60 gm. daily, and

the acidity of the gastric secretion had risen to above its original level.

Case 3. N.C.L. (Fig.V.)

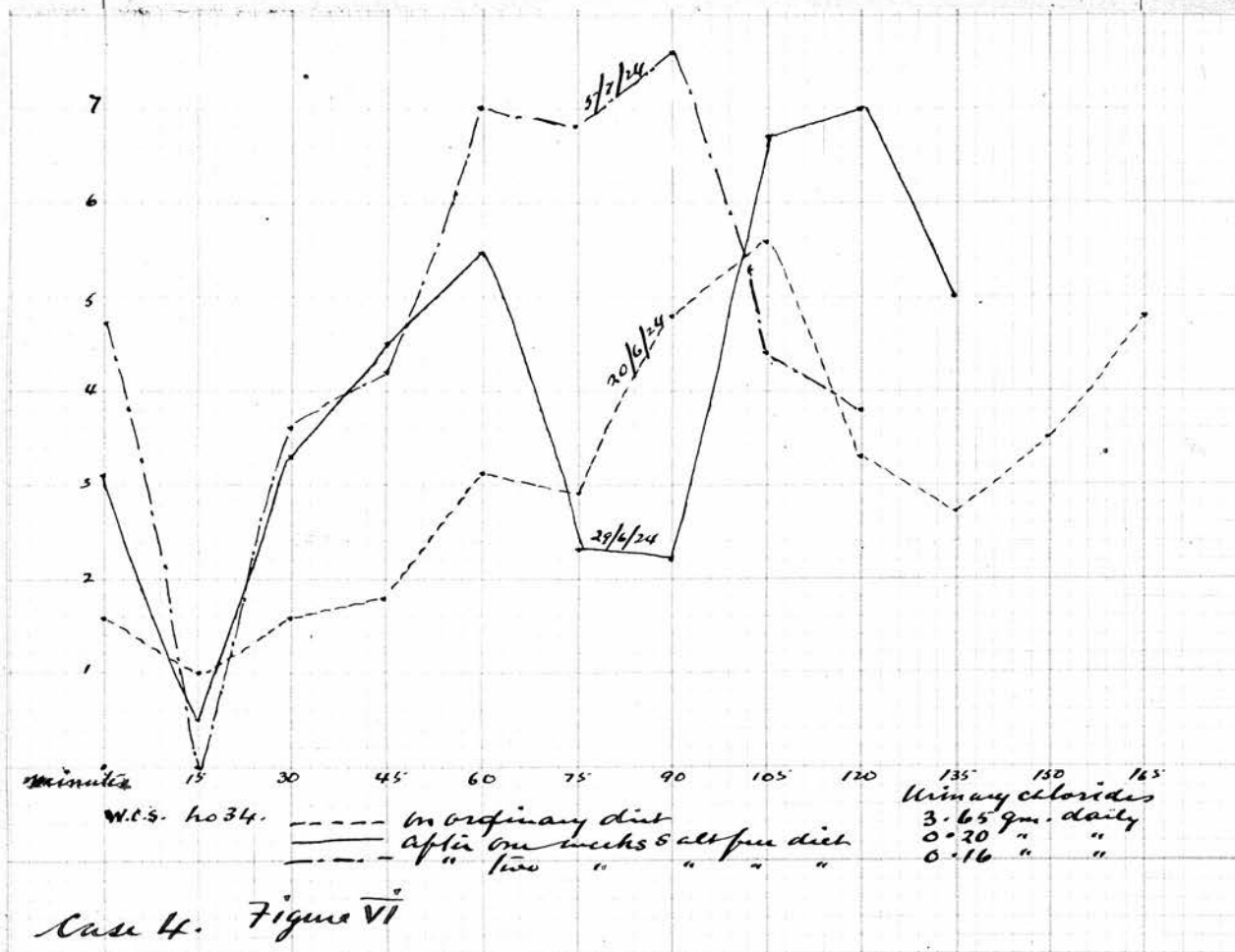


Case 3. Figure V

The result in this case is not so definite, possibly because of the shorter time of experiment. After one week the acidity curve was lower than the

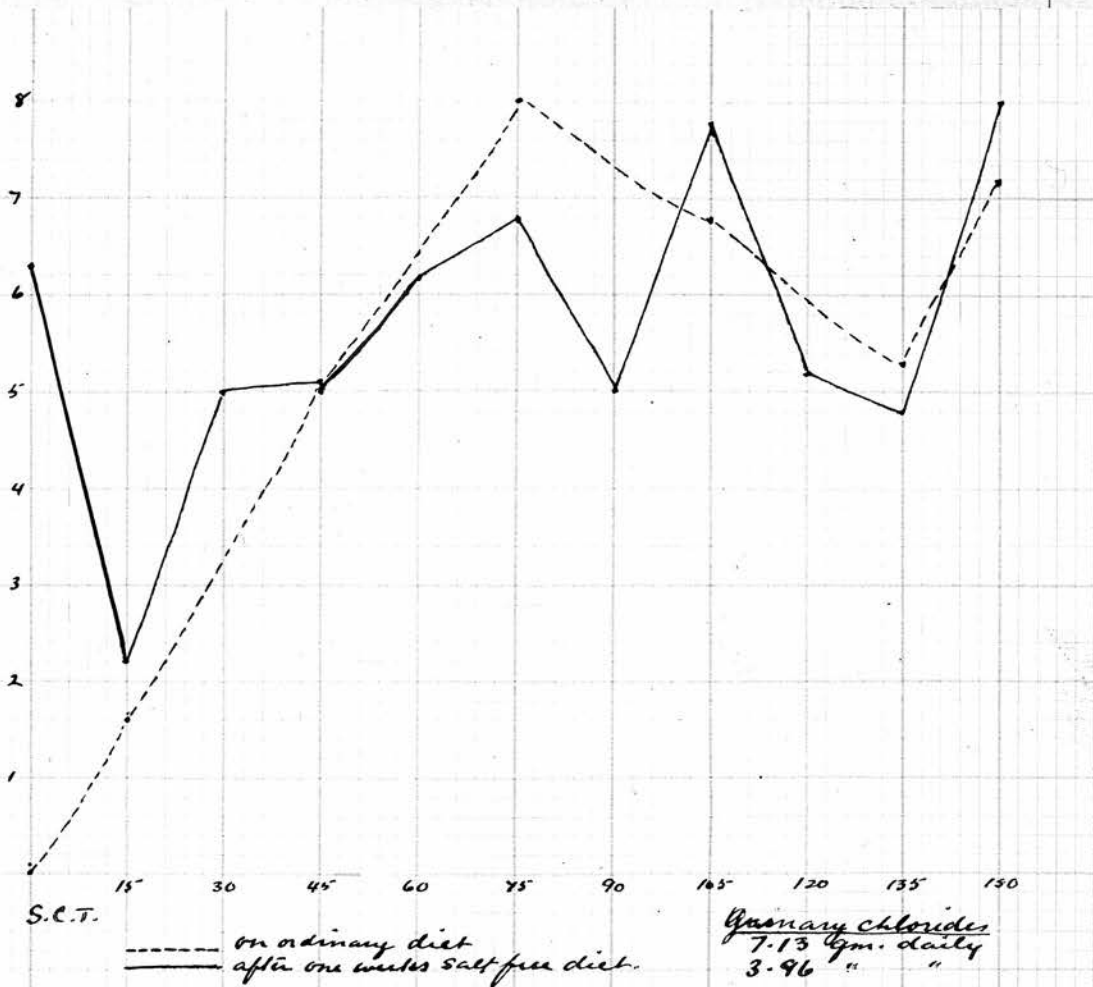
original curve at most points, but higher at some points. After two weeks the urinary chlorides had risen to 1.57 gm. daily and the acidity curve was on the whole higher than originally.

Case 4. W.C.S. (Fig.VI.)



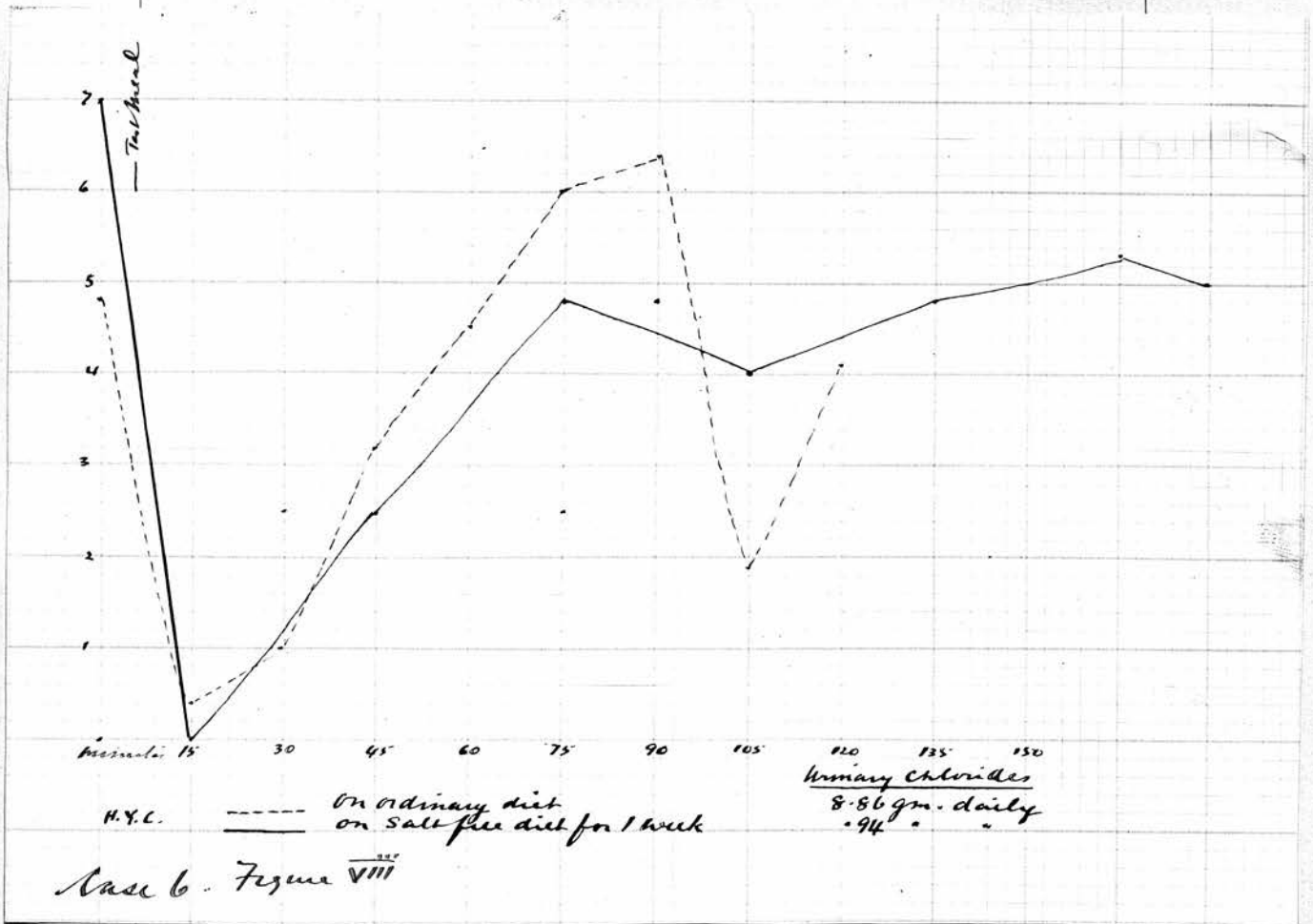
In this case, although the urinary chlorides fell to the low figures of .20 and .16 gms. daily, there was if anything an increase in the gastric acidity.

Case 5. S.C.T. (Fig.VII.)

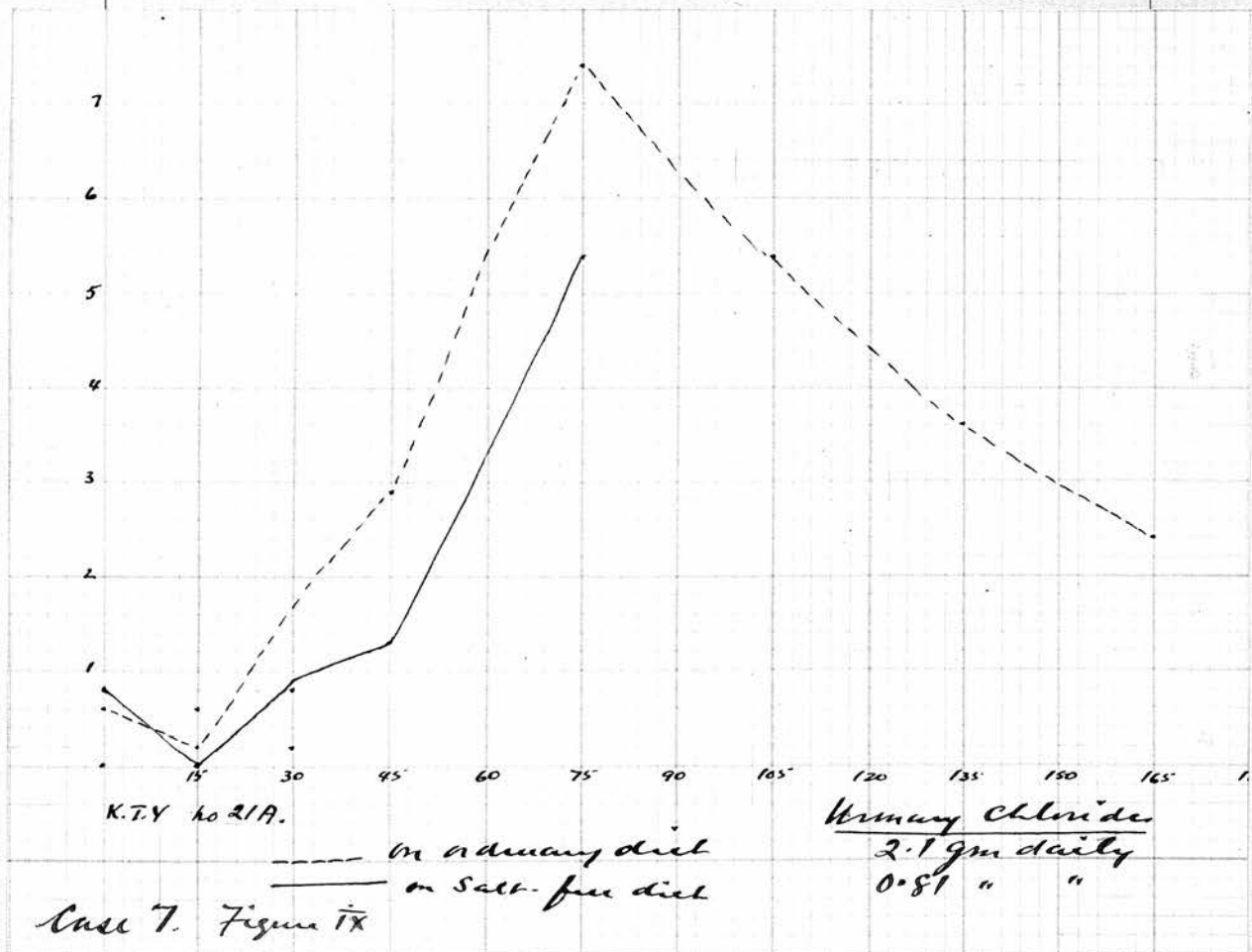


Case 5. Figure VII

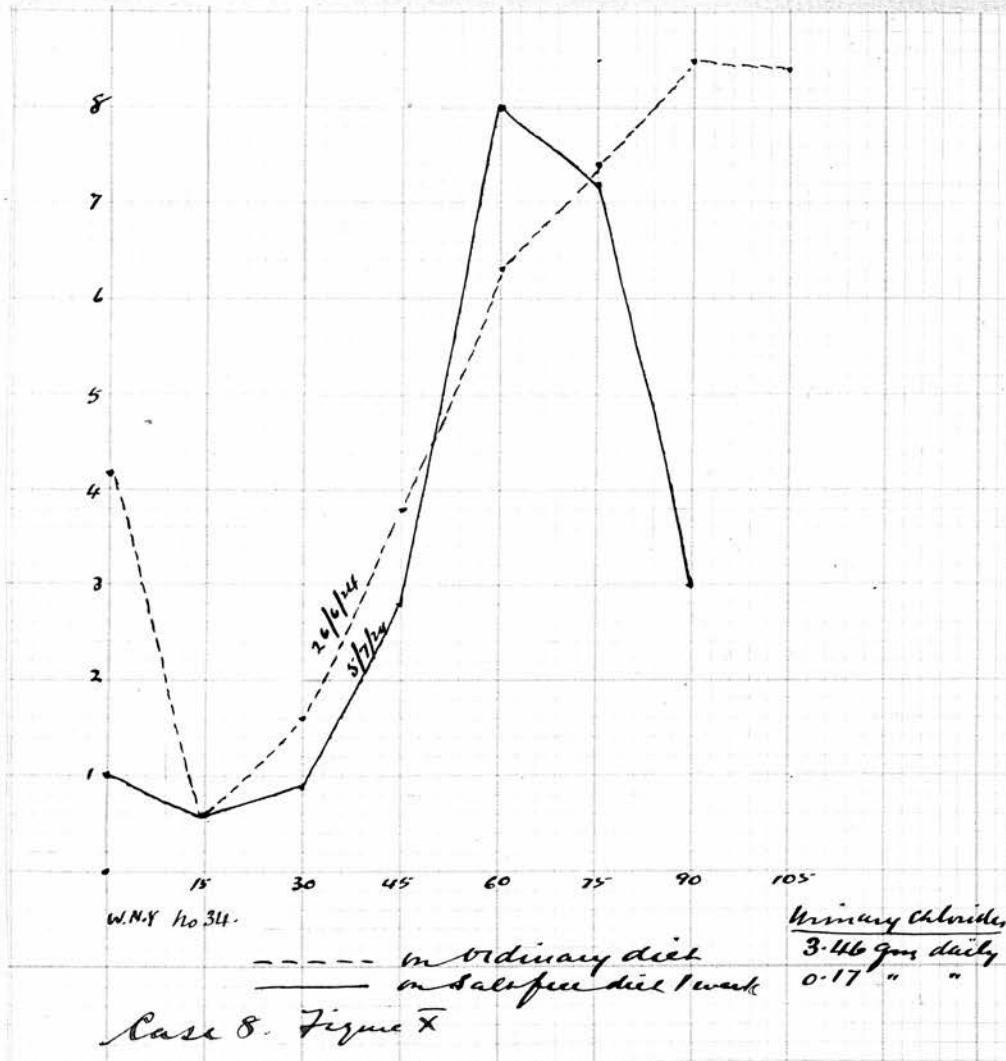
In this case there was practically no change in the acidity, but the urinary chlorides, after one week of salt free diet, fell only to 3.96 gms. daily. It may be presumed that the subject of this experiment was not conscientious in his abstinence from salt.

Case 6. H.Y.C. (Fig.VIII.)

This case was on salt-free diet for five days.
The gastric acidity shows little change.

Case 7. K.T.Y. (Fig.IX.)

This case was on salt free diet for one week. The free acidity shows a diminution. Emptying of the stomach was much more rapid (75 minutes compared with 165 minutes). The reading of 5.4 on the lower curve at 75 minutes is probably inaccurate, as only a small quantity of gastric contents was obtained.

Case 8. W.N.Y. (Fig.X.)

This subject, who was on salt free diet for nine days, showed a diminution of free acidity at most points of the curve.

The curves shown above show amounts of free hydrochloric acid present in the gastric contents. Total acidity was also determined in each case, but as the curves obtained correspond fairly closely in general outline, they are not shown as it would only complicate the diagrams.

GENERAL INFERENCES FROM THESE EXPERIMENTS.

The number of cases examined is unfortunately rather too small, and in most cases the period of time under observation too short to permit of absolutely definite conclusions being drawn.

With this in mind, the following general inferences may be made.

- (1) If a salt free diet be taken for a sufficiently long period of time, say, four or five weeks, a definite considerable diminution of the acidity of the gastric contents is observed.
- (2) In cases where the period of time is shorter, there is usually a less marked diminution in the acidity of the gastric contents, although this is not absolutely constant (see Case 4).

- (3) The minimum amount of salt required daily to maintain the normal acidity of the gastric secretion is not definitely determined by these experiments, but most of the results tend to show that it is in between 1 and 2 grams.
- (4) With the exception of the changes in the gastric juice and in the urine, none of the subjects of these experiments showed any other effects. Their general state of health remained unchanged and their only complaint was that their food was tasteless and insipid.

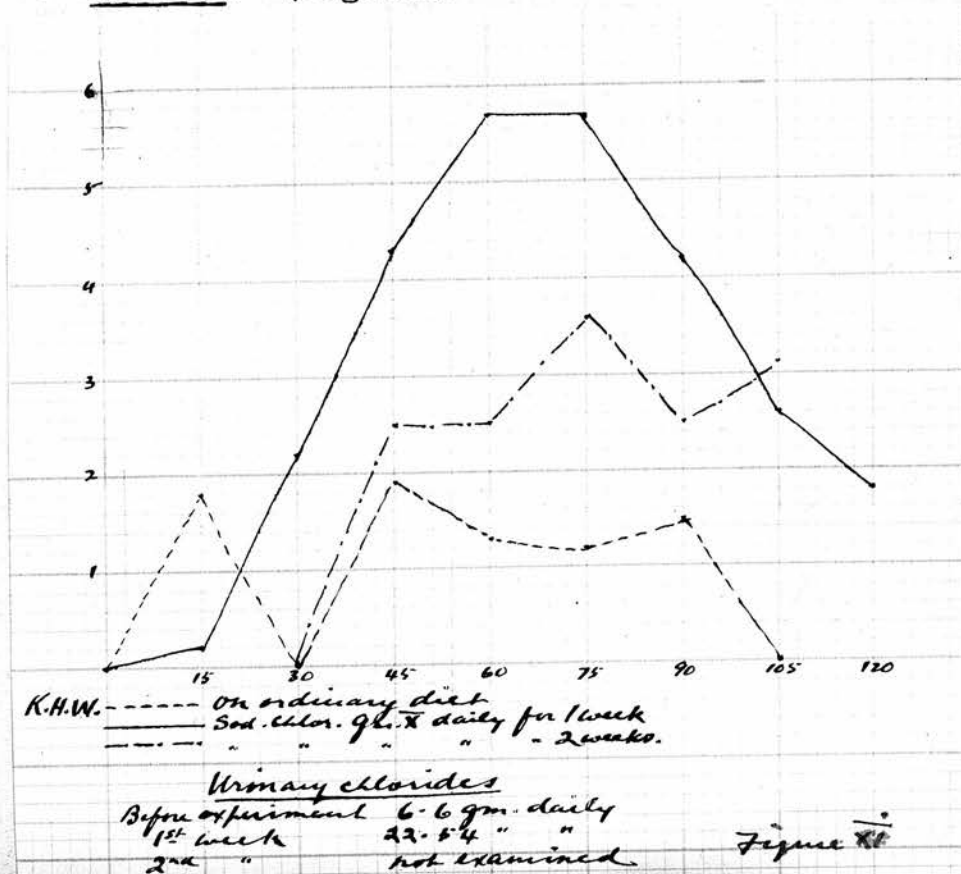
In connection with these experiments on low chloride diets, a case may be reported of a patient suffering from parenchymatous nephritis with oedema who was treated by a salt free diet for six or seven weeks. At the end of this time the writer found complete absence of hydrochloric acid in the gastric juice and the total acidity was very low. Unfortunately the gastric juice was not examined before the salt-free diet was begun. One is very doubtful whether or not to ascribe this achlorhydria to the low chloride-intake. It is well known that in this type of nephritis, there is retention of chlorides in the body, and it is therefore uncertain that the achlorhydria was due to a deficiency of chlorides. F. C. MacLean (1915) found that the plasma chlorides were increased in renal disturbances.

CASES OF HYPOCHLORHYDRIA TREATED BY LARGE DOSES OF
SODIUM CHLORIDE.

With a view to determining whether or not the condition of deficient gastric secretion could be improved by increasing the chloride content of the food, the writer performed the following experiments.

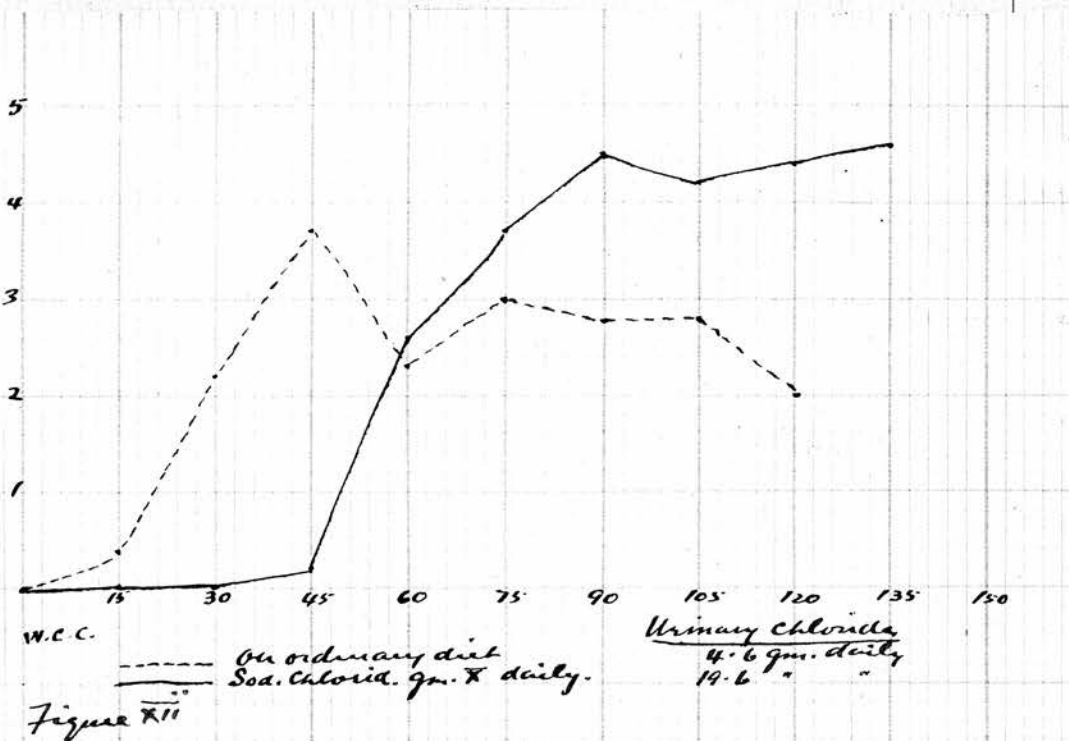
Case I. A man suffering from chronic alcoholic gastritis, with complete absence of free hydrochloric acid and total acidity of 21, was given sodium chloride 10 grams daily for twelve days. At the end of this period there was no increase in the acidity of the gastric contents. This was the expected result, as the condition was due, not to any deficiency of chlorides, but to a fault in the secreting glands.

Case II. (Fig.XI.)



A man suffering from pleurisy with effusion and slight chronic gastritis, on receiving 10 grams of sodium chloride daily for one week, showed a great increase of the acidity of the gastric contents. At the end of the second week the acidity had fallen somewhat, but was still considerably higher than originally.

Case III. (Fig.XII.)



A case of chronic gastritis treated with 10 gms. of sodium chloride daily. After one week the gastric contents showed a slight increase in acidity - although the original acidity had not been unduly low.

Case IV. A case (diagnosis uncertain) whose original gastric examination showed acidity to be normal, was given sodium chloride gm.X. daily for one week. At the end of that time there was no essential change in the gastric contents.

It is probably not permissible to draw conclusions from such a short series of cases, but the results obtained, especially in Case II., are suggestive. The writer hopes to pursue further this line of investigation when opportunity occurs.

There are several ways in which chlorides in the food may conceivably affect the gastric secretion.

- (1) They may have a directly stimulating influence on the gastric mucosa.
- (2) They may act in a reflex manner, e.g., as condiments.
- (3) They may have a stimulating influence on the general metabolism. This is the theory of Voit, but has not been confirmed.
- (4) They may act in a physical way, e.g. by osmosis.
- (5) Changes in the amount of chlorides in the food may cause changes in the amount of hydrochloric acid secreted by the stomach through

alterations in the chloride content of the blood serum or of the tissues generally.

We shall consider these possibilities seriatim.

(1) There is little reason for believing that chlorides exert a direct influence on the gastric mucosa in such a way as to cause changes in the secretion, notwithstanding Frouin's experimental result described on page 20. Of course saline solutions produce effects in the cells of the gastric mucosa similar to those produced on all living cells. That is to say, a hypotonic saline solution will cause temporary swelling and a hypertonic solution will cause shrinkage of the gastric cells.

Cushny⁽¹⁷⁾ states that strongly hypertonic saline solution may cause vomiting and other disorders of digestion, but in the present paper we are not considering highly concentrated solutions.

There is reason to believe that even in small quantities salt does not necessarily improve the gastric function. Thus Hamburger⁽¹⁸⁾ states that a neutral solution of sodium chloride rapidly destroys pepsin, but only in the absence of free acid.

Cushny holds that small quantities of salt have been found to lessen the acidity of the gastric juice.

Poulssen⁽¹⁹⁾ states that digestion in the stomach is hindered a little by salt and that the acidity of the contents of the stomach is decreased, as there is

secretion of fluids with an alkaline reaction, especially if the salt solution is not very weak.

There is thus considerable reason to hold that the direct influence of chlorides on the gastric secretion is, if any, a harmful one.

(2) Most authorities agree that salt in the food acts on the gastric secretion reflexly and tends to increase the flow. This action is very similar to that of the bitters.

Dapper⁽²⁰⁾ found that the hydrochloric acid of the gastric juice was increased in some persons and diminished in others by mineral waters containing sodium chloride as their chief ingredient. He holds that these waters have no effect on secretion directly, but may alter it by changing the nutrition of the gastric mucous membrane, or by arousing secretion reflexly by their taste.

(3) Salt in the food has probably little or no direct influence on general metabolism - and thus could not influence the gastric secretion in this way (Poulssen).

(4) The ingestion of large quantities of salt would tend to render the blood temporarily hypertonic, and as a consequence to increase the total volume of blood. This change is associated with a rise of

capillary pressure in the abdominal viscera and might thus increase the flow of gastric juice (Dixon⁽²¹⁾).

(5) We have seen that the chloride content of the blood plasma is remarkably constant. However, in conditions of chloride starvation, the kidneys continue to excrete chlorides in quantities of from 0.6 - 0.9 grams per day, so that the total amount of chlorine in the body must be reduced, and it is probable that the blood plasma shares in this loss to some extent. It is conceivable that a reduced chlorine content in the blood plasma would adversely affect the hydrochloric acid secretion of the stomach.

When an increased quantity of salt is taken in the food, the surplus is excreted fairly quickly by the kidneys, but the excretion lags somewhat behind the intake and a state of equilibrium is not reached until after three or four days. It is possible that meantime the increased chloride content of the tissues, including the blood, might cause an increased secretion of hydrochloric acid by the stomach. Rosemann⁽²²⁾ found that in dogs the entire chlorine content of the body was increased by 100% when they were given a highly salted diet.

The cases in which one would expect an increased intake of chlorides to affect beneficially the gastric secretion are those in which there was previously

a deficient intake of chlorides. It is not to be expected that cases whose intake of chlorides was already sufficient would benefit in this way, except perhaps from the slight beneficial influence of salt as a condiment. Cases in which there was atrophy of the secretory glands could not be expected to benefit from this treatment.

CONCLUSIONS.

- (1) The amount of chlorides excreted daily in the urine of Northern Chinese is much smaller than in Western peoples.
- (2) The average hydrochloric acid content of the gastric secretion does not differ from that of Western peoples.
- (3) In the case of persons on their ordinary diet, there was no evident relation between the quantity of urinary chlorides (i.e. between the ingested chlorides) and the hydrochloric acid content of the gastric juice.
- (4) In persons fed for a sufficiently long time on a low chloride diet, there is a considerable diminution in the acidity of

gastric juice. This fact should be borne in mind when patients are treated on chlorine free diets over long periods of time.

- (5) In certain patients with hypo-chlorhydria, the addition of large amounts of sodium chloride to the diet results in an increase in the acidity of the gastric juice. In other cases there is no evident change in the gastric secretion.
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